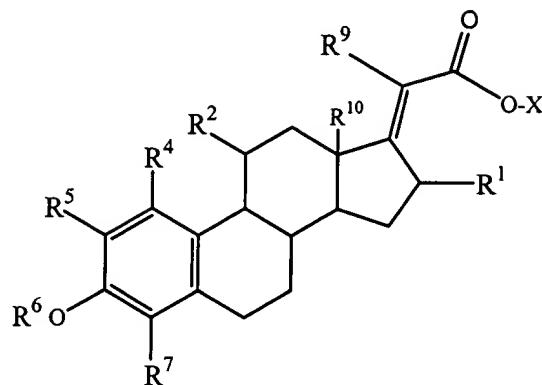


**WE CLAIM:**

1. A compound having the structural formula (I)

(I)



wherein:

X is lower hydrocarbyl;

R<sup>1</sup> is CR<sup>11</sup>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> are hydrogen or lower alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, hydroxyl, alkyl, -OR<sup>13</sup>, and -SR<sup>13</sup>

wherein R<sup>13</sup> is alkyl;

R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> are independently selected from the group consisting of hydrogen and lower alkyl;

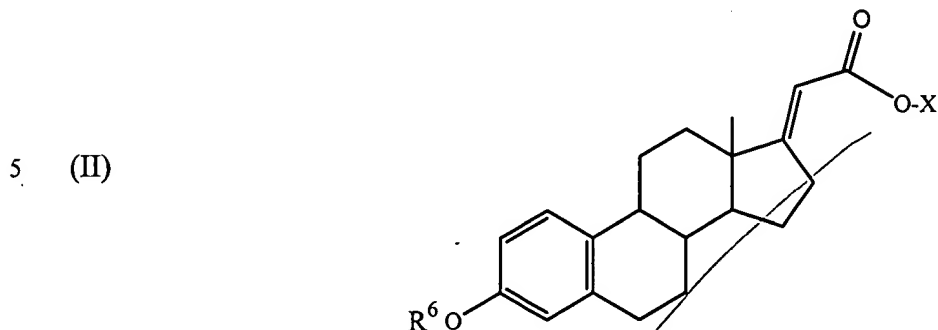
R<sup>9</sup> is hydrogen or hydrocarbyl; and

R<sup>10</sup> is methyl or ethyl.

*07/280,990*

-52-

2. The compound of claim 1, having the structural formula (II)



wherein:

10 X is lower alkyl; and

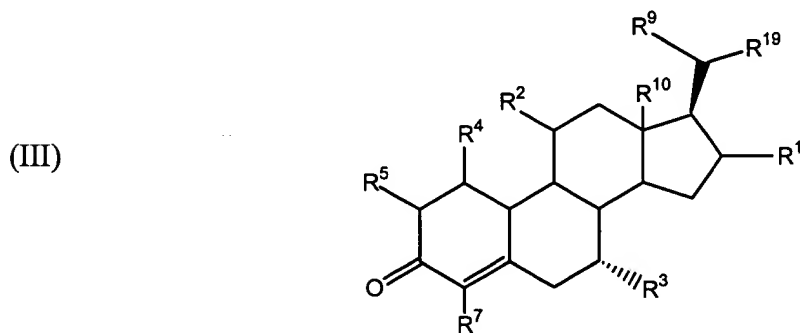
$R^6$  is selected from the group consisting of hydrogen and lower alkyl.

3. The compound of claim 2, wherein  $R^6$  is hydrogen.

- 15 4. The compound of claim 2, wherein  $R^6$  is lower alkyl.

5. The compound of claim 4, wherein  $R^6$  is methyl.

- 20 6. A compound having the structural formula (III)



wherein:

30  $R^1$  is  $CR^{11}R^{12}$ , wherein  $R^{11}$  and  $R^{12}$  are hydrogen or lower alkyl;

$R^2$  is selected from the group consisting of hydrogen, hydroxyl, alkyl,  $-OR^{13}$ , and  $-SR^{13}$

*Ch 6-13*  
*selected*

wherein  $R^{13}$  is alkyl;

$R^3$  is selected from the group consisting of hydrogen and hydrocarbyl;

$R^4$ ,  $R^5$ , and  $R^7$  are independently hydrogen or lower alkyl;

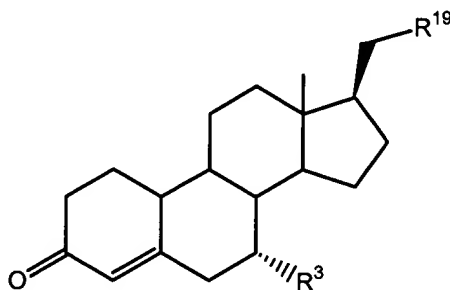
$R^9$  is hydrogen or hydrocarbyl;

$R^{10}$  is methyl or ethyl; and

$R^{19}$  is hydroxyl, hydroxymethyl, protected hydroxyl, protected hydroxymethyl, activated hydroxyl, or activated hydroxymethyl.

7. The compound of claim 6, having the structural formula (IV)

(IV)



wherein:

$R^3$  is hydrogen or lower alkyl; and

$R^{19}$  is hydroxyl, hydroxymethyl, -O-acetyl, or -O-tetrahydropyranyl.

8. The compound of claim 7, wherein  $R^3$  is hydrogen or methyl, and  $R^{19}$  is hydroxymethyl.

9. The compound of claim 8, wherein  $R^3$  is hydrogen.

10. The compound of claim 8, wherein  $R^3$  is methyl.

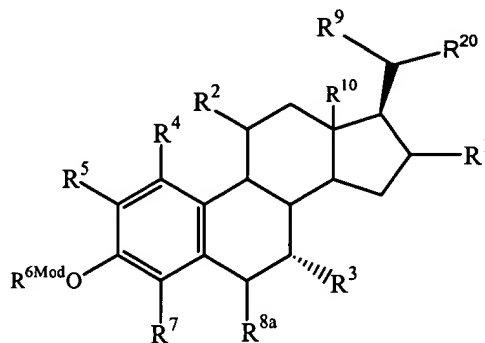
11. The compound of claim 7, wherein  $R^3$  is hydrogen or methyl, and  $R^{19}$  is hydroxyl.

12. The compound of claim 11, wherein  $R^3$  is hydrogen.

13. The compound of claim 11, wherein  $R^3$  is methyl.

14. A compound having the structural formula (V)

(V)



wherein:

$R^1$  is hydrogen or  $CR^{11}R^{12}$ , wherein  $R^{11}$  and  $R^{12}$  are hydrogen or lower alkyl;

$R^2$  is selected from the group consisting of hydrogen, hydroxyl, alkyl,  $-OR^{13}$ , and  $-SR^{13}$

wherein  $R^{13}$  is alkyl;

$R^3$  is selected from the group consisting of hydrogen and hydrocarbyl;

$R^4$ ,  $R^5$ , and  $R^7$  are independently selected from the group consisting of hydrogen and lower alkyl;

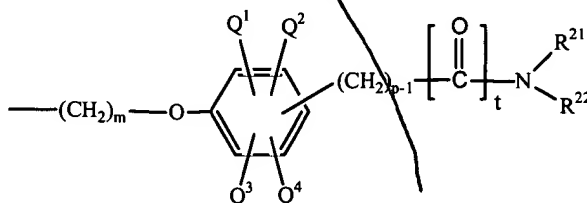
$R^{6Mod}$  is selected from the group consisting of hydrogen, alkyl, acyl,  $-C(O)$ -aryl,  $-C(O)$ -alkyl, hydroxyl-protecting groups, and hydroxyl-activating groups;

$R^{8a}$  is selected from the group consisting of hydrogen, hydroxyl, oxo, and  $-OR^{18}$  wherein  $R^{18}$  is lower alkyl or lower acyl;

$R^9$  is hydrogen or alkyl;

$R^{10}$  is methyl or ethyl; and

$R^{20}$  is hydroxyl, hydroxymethyl, protected hydroxyl, protected hydroxymethyl, activated hydroxyl, activated hydroxymethyl, or

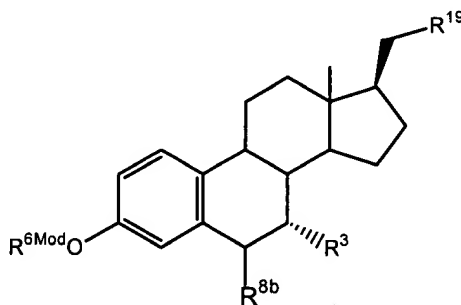


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cost  
in which m is zero or 1, p is an integer in the range of 1 to 7 inclusive, t is zero or 1, with the proviso that when R<sup>8a</sup> is oxo, t is 1, and when R<sup>8a</sup> is hydrogen, t is zero, and R<sup>21</sup> and R<sup>22</sup> are lower alkyl or are linked together to form a five- or six-membered heterocycloalkyl ring; and

Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup>, and Q<sup>4</sup> are independently selected from the group consisting of hydrogen, hydroxyl, carboxyl, alkoxy, alkyl, halogen, amino, and alkyl-substituted amino.

15. The compound of claim 14, having the structural formula (VI)

(VI)



wherein:

R<sup>3</sup> is hydrogen or lower alkyl;

R<sup>6Mod</sup> is hydrogen or a hydroxyl-protecting group;

R<sup>8b</sup> is selected from the group consisting of hydrogen, hydroxyl, and oxo; and

R<sup>19</sup> is hydroxyl, hydroxymethyl, protected hydroxyl, protected hydroxymethyl, activated hydroxyl, or activated hydroxymethyl.

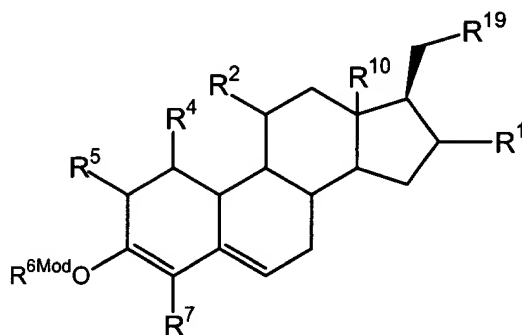
16. The compound of claim 15, wherein R<sup>3</sup> is hydrogen or methyl, R<sup>6Mod</sup> is hydrogen or lower alkyl, R<sup>8b</sup> is oxo, and R<sup>19</sup> is hydroxyl, hydroxymethyl, -O-acetyl, or -O-tetrahydropyranyl.

17. The compound of claim 16, wherein R<sup>3</sup> is methyl.

A2  
SUB  
18. The compound of claim 17, wherein R<sup>6Mod</sup> is isopropyl.

19. A compound having the structural formula (XXVII)

5 (XXVII)



10 wherein:

$R^1$  is hydrogen or  $CR^{11}R^{12}$ , wherein  $R^{11}$  and  $R^{12}$  are hydrogen or lower alkyl;

$R^2$  is selected from the group consisting of hydrogen, hydroxyl, alkyl,  $-OR^{13}$ , and  $-SR^{13}$  wherein  $R^{13}$  is alkyl;

15  $R^4$ ,  $R^5$ , and  $R^7$  are independently selected from the group consisting of hydrogen and lower alkyl;

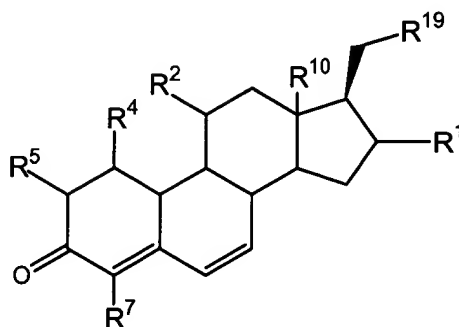
$R^{6Mod}$  is selected from the group consisting of hydrogen, alkyl, acyl,  $-C(O)-aryl$ ,  $-C(O)-alkyl$ , hydroxyl-protecting groups, and hydroxyl-activating groups;

$R^{10}$  is methyl or ethyl; and

20  $R^{19}$  is hydroxyl, hydroxymethyl, protected hydroxyl, protected hydroxymethyl, activated hydroxyl, or activated hydroxymethyl.

20. A compound having the structural formula (XXVIII)

(XXVIII)



wherein:

$R^1$  is hydrogen or  $CR^{11}R^{12}$ , wherein  $R^{11}$  and  $R^{12}$  are hydrogen or lower alkyl;

$R^2$  is selected from the group consisting of hydrogen, hydroxyl, alkyl,  $-OR^{13}$ , and  $-SR^{13}$

wherein  $R^{13}$  is alkyl;

$R^4$ ,  $R^5$ , and  $R^7$  are independently selected from the group consisting of hydrogen and

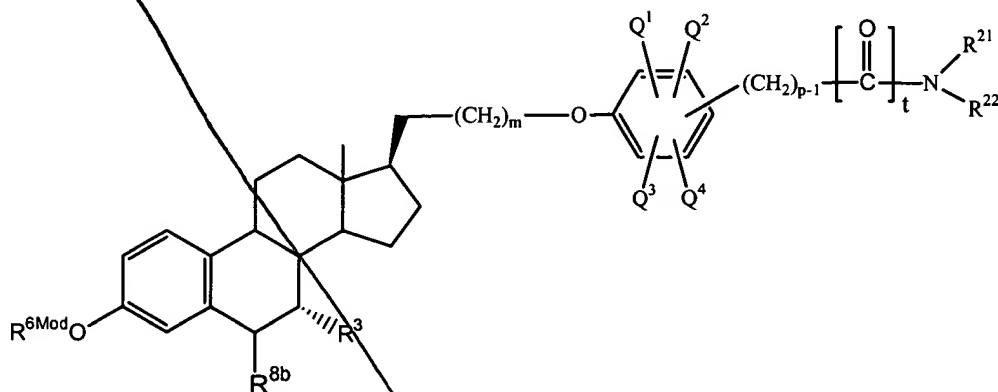
lower alkyl;

$R^{10}$  is methyl or ethyl; and

$R^{19}$  is hydroxyl, hydroxymethyl, protected hydroxyl, protected hydroxymethyl, activated hydroxyl, or activated hydroxymethyl.

21. A compound having the structural formula (VII)

(VII)



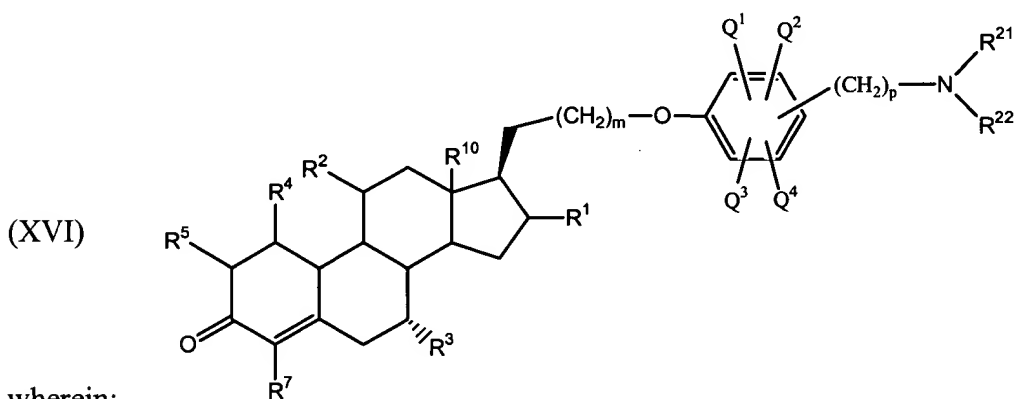
wherein:

$R^3$  is hydrogen or hydrocarbyl;

-58-

A3  
Cest  
R<sup>6Mod</sup> is selected from the group consisting of hydrogen, alkyl, acyl, -C(O)-aryl, and  
-C(O)-alkyl, hydroxyl-protecting groups, and hydroxyl-activating groups;  
R<sup>8b</sup> is selected from the group consisting of hydrogen, hydroxyl, and oxo;  
m is zero or 1;  
p is an integer in the range of 1 to 7 inclusive;  
t is zero or 1, with the proviso that when R<sup>8a</sup> is oxo, t is 1, and when R<sup>8a</sup> is hydrogen, t  
is zero, and;  
R<sup>21</sup> and R<sup>22</sup> are lower alkyl or are linked together to form a five- or six-membered  
heterocycloalkyl ring; and  
Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup>, and Q<sup>4</sup> are independently selected from the group consisting of hydrogen,  
hydroxyl, carboxyl, alkoxy, alkyl, halogen, amino, and alkyl-substituted amino.

22. A compound having the structural formula (XVI)



wherein:

R<sup>1</sup> is CR<sup>11</sup>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> are hydrogen or lower alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, hydroxyl, alkyl, -OR<sup>13</sup>, and -SR<sup>13</sup>

wherein R<sup>13</sup> is alkyl;

R<sup>3</sup> is hydrogen or hydrocarbyl;

R<sup>4</sup> and R<sup>5</sup> are independently selected from the group consisting of hydrogen and lower  
alkyl;

R<sup>7</sup> is hydrogen or lower alkyl;

R<sup>10</sup> is methyl or ethyl;

m is zero or 1;



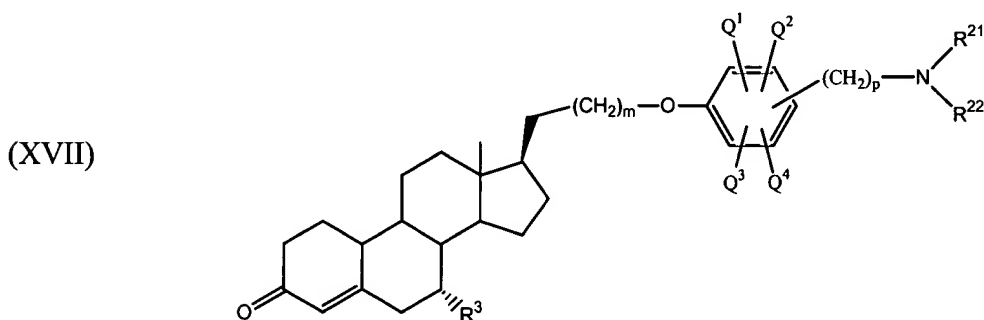
-59-

p is an integer in the range of 1 to 7 inclusive;

R<sup>21</sup> and R<sup>22</sup> are lower alkyl or are linked together to form a five- or six-membered heterocycloalkyl ring; and

Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup>, and Q<sup>4</sup> are independently selected from the group consisting of hydrogen, hydroxyl, carboxyl, alkoxy, alkyl, halogen, amino, and alkyl-substituted amino, or a pharmacologically acceptable acid addition salt thereof.

23. The compound of claim 22, having the structural formula (XVII)



wherein:

m is zero or 1;

p is an integer in the range of 1 to 7 inclusive;

R<sup>3</sup> is hydrogen or lower alkyl;

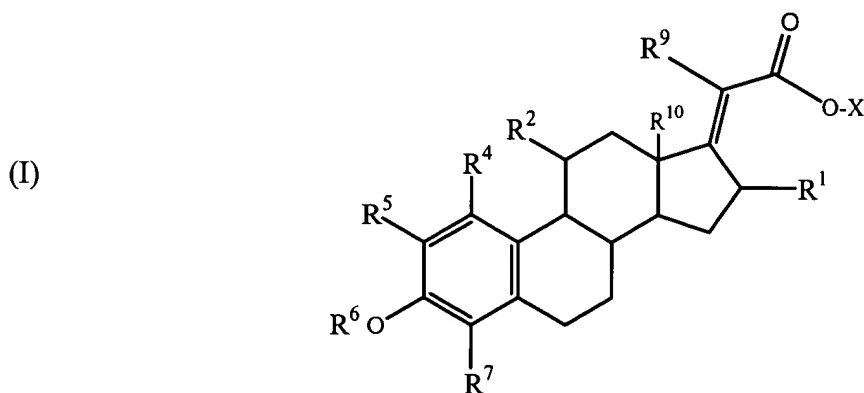
R<sup>21</sup> and R<sup>22</sup> are lower alkyl or are linked together to form a five- or six-membered heterocycloalkyl ring; and

Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup>, and Q<sup>4</sup> are independently selected from the group consisting of hydrogen, hydroxyl, carboxyl, alkoxy, alkyl, halogen, amino, and alkyl-substituted amino, or a pharmacologically acceptable acid addition salt thereof.

24. The compound of claim 21, wherein R<sup>3</sup> is lower alkyl.

25. The compound of claim 22, wherein R<sup>3</sup> is methyl.

26. A method for synthesizing 21-hydroxy-19-norpregna-4-en-one and substituted analogs thereof, comprising treating a starting material having the structural formula (I)



with an alkali metal in the presence of ammonia or an alkylamine, wherein, in formula (I),

X is lower hydrocarbyl;

R<sup>1</sup> is CR<sup>11</sup>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> are hydrogen or lower alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, hydroxyl, alkyl, -OR<sup>13</sup>, and -SR<sup>13</sup>

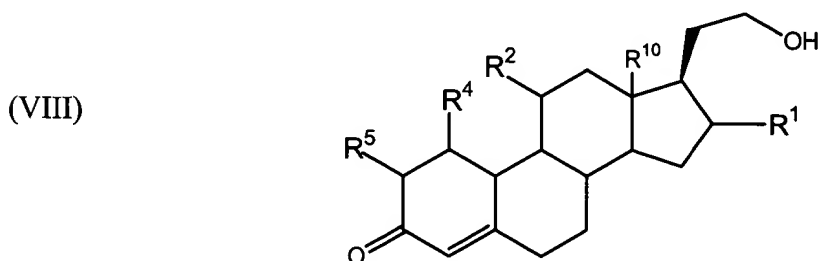
wherein R<sup>13</sup> is alkyl;

R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> are independently selected from the group consisting of hydrogen and lower alkyl;

R<sup>9</sup> is hydrogen or hydrocarbyl; and

R<sup>10</sup> is methyl or ethyl, resulting in a reaction product having the structural formula

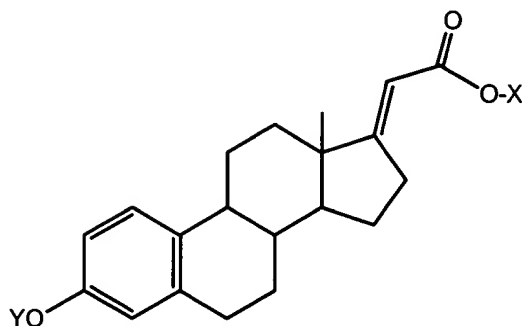
(VIII)



-61-

27. A method for synthesizing 21-hydroxy-19-norpregna-4-en-3-one, comprising treating (IX)

(IX)

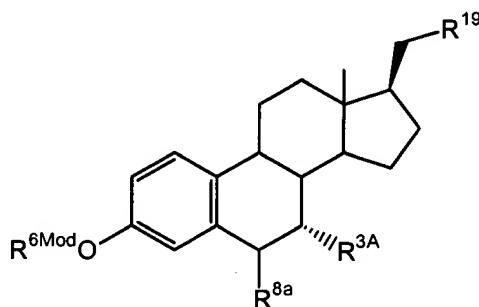


wherein X and Y are independently lower alkyl, with an alkali metal in the presence of ammonia or an alkylamine.

28. A method for synthesizing a 7-alkyl-6-keto-1,3,5(10) estratriene, comprising contacting a 19-norpregna-4-en-3-one with gaseous oxygen in the presence of base, followed by reaction of the intermediate so provided with an alkyl halide.

29. A method for synthesizing a 7-alkyl-6-keto-1,3,5(10) estratriene having the structural formula (VIa)

(VIa)



wherein:

$\text{R}^{3A}$  is lower alkyl;

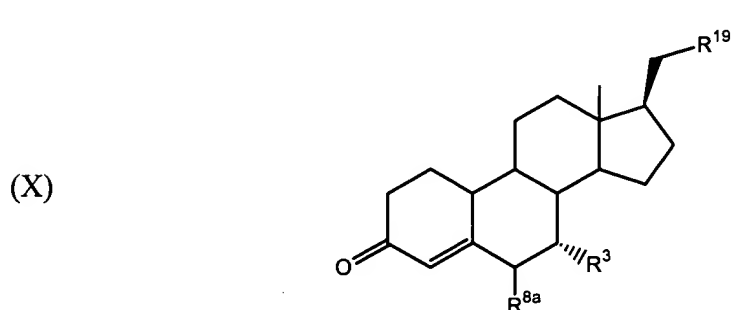
$\text{R}^{6\text{Mod}}$  is hydrogen or a hydroxyl-protecting group;

$\text{R}^{8a}$  is hydrogen or oxo; and

-62-

$R^{19}$  is hydroxyl, hydroxymethyl, protected hydroxyl, or protected hydroxymethyl, the method comprising the steps of

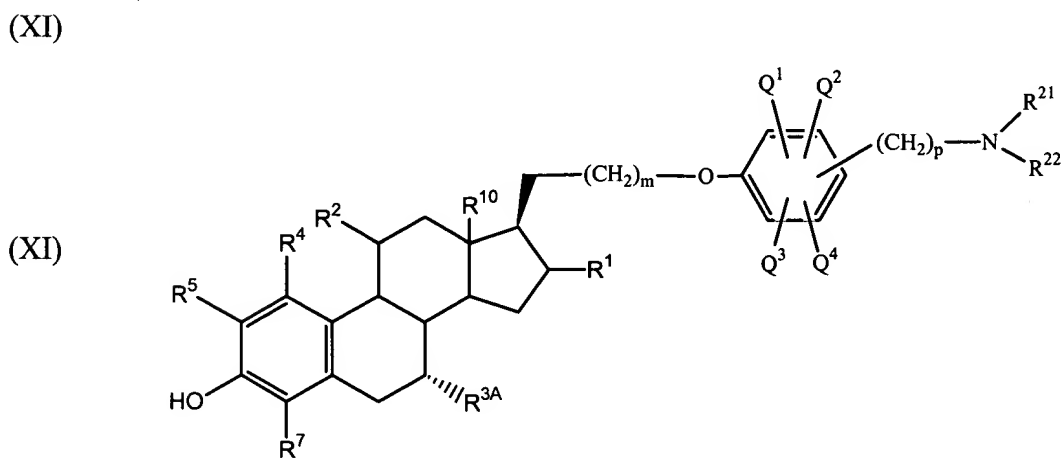
- (a) contacting the 19-norpregna-4-en-3-one (X)



with oxygen in the presence of a base;

- (b) protecting the 3-hydroxyl group thus formed with a protecting group, and  
(c) treating the 3-hydroxyl-protected intermediate with an alkyl halide.

15  
30. A method for synthesizing an anti-estrogenic steroid having the structural formula



wherein:

$R^1$  is  $CR^{11}R^{12}$ , wherein  $R^{11}$  and  $R^{12}$  are hydrogen or lower alkyl, and when  $R^1$  is absent,  $R^1$  is hydrogen or alkyl;

$R^2$  is selected from the group consisting of hydrogen, hydroxyl, alkyl, and  $-OR^{13}$

30 wherein  $R^{13}$  is alkyl;

-63-

$R^{3A}$  is lower alkyl;

$R^4$ ,  $R^5$ ,  $R^6$ , and  $R^7$  are independently selected from the group consisting of hydrogen and lower alkyl; and

$R^{10}$  is methyl or ethyl;

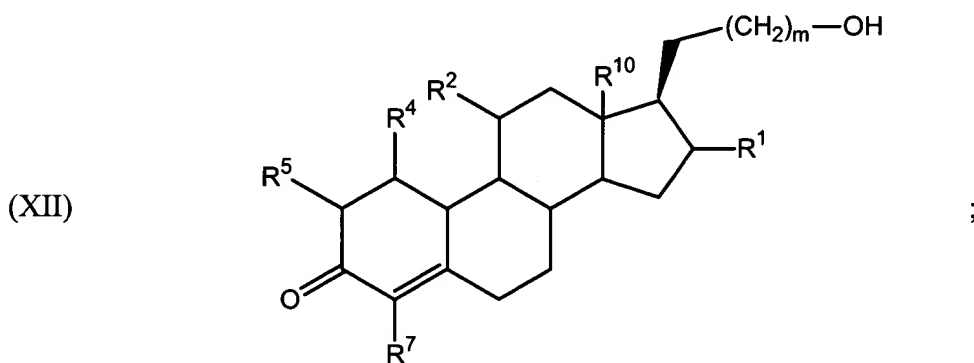
$m$  is zero or 1;

$p$  is an integer in the range of 1 to 7 inclusive;

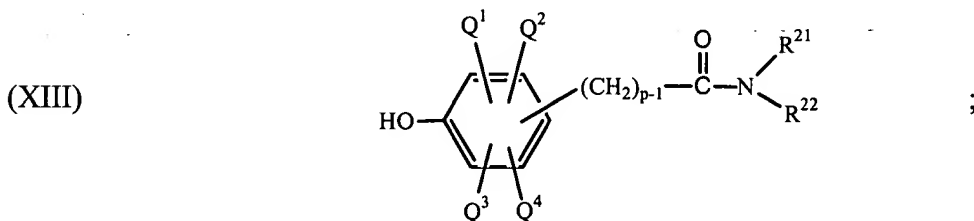
$R^{21}$  and  $R^{22}$  are lower alkyl or are linked together to form a five- or six-membered heterocycloalkyl ring; and

$Q^1$ ,  $Q^2$ ,  $Q^3$ , and  $Q^4$  are independently selected from the group consisting of hydrogen, hydroxyl, carboxyl, alkoxy, alkyl, halogen, amino, and alkyl-substituted amino, said method comprising:

(a) providing a starting material having the structural formula (XII)



(b) converting the -OH group to an -O-LG moiety wherein LG is a leaving group displaceable by nucleophilic attack, and displacing LG by reaction with a hydroxyl-containing compound having the structural formula (XIII)



(c) oxidizing the A ring and providing a 6-keto moiety by exposure to gaseous oxygen in the presence of base;

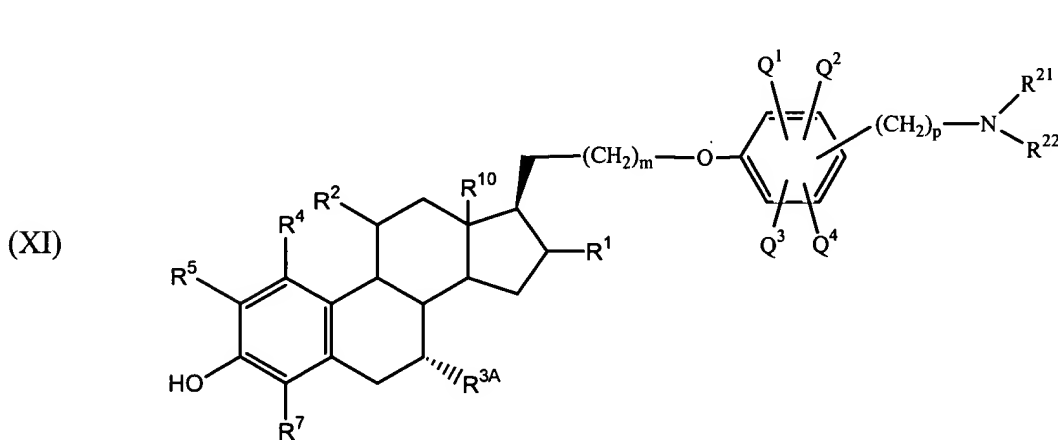
(d) protecting the 3-hydroxyl group with a protecting group;

(e) contacting the product of step (d) with an alkyl halide, to provide a 7 $\alpha$ -alkyl substituent; and

(f) reducing the compound so provided to remove all keto moieties, with the proviso that steps (c) and (d) may occur prior to or simultaneously with step (b).

31. The method of claim 30, further including (g) treating the product of step (f) with an acid to produce an acid addition salt.

32. A method for synthesizing an anti-estrogenic steroid having the structural formula (XI)



wherein:

R<sup>1</sup> is CR<sup>11</sup>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> are hydrogen or lower alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, hydroxyl, alkyl, and -OR<sup>13</sup>

wherein R<sup>13</sup> is alkyl;

R<sup>3A</sup> is lower alkyl;

R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are independently selected from the group consisting of hydrogen and

lower alkyl; and

-65-

$R^{10}$  is methyl or ethyl.

m is zero or 1;

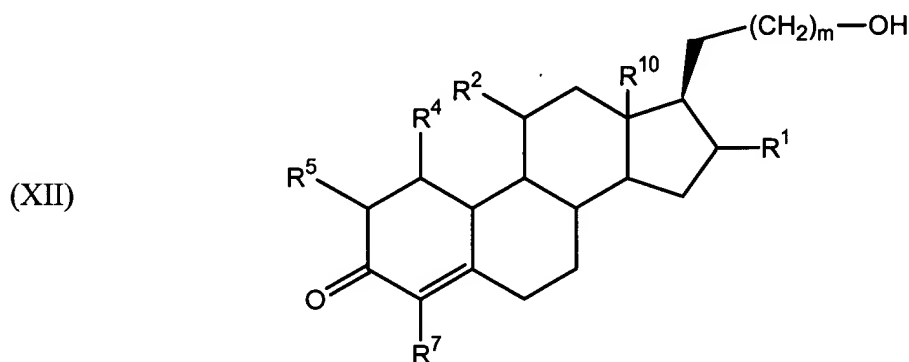
p is an integer in the range of 1 to 7 inclusive;

$R^{21}$  and  $R^{22}$  are lower alkyl or are linked together to form a five- or six-membered

heterocycloalkyl ring; and

$Q^1$ ,  $Q^2$ ,  $Q^3$ , and  $Q^4$  are independently selected from the group consisting of hydrogen, hydroxyl, carboxyl, alkoxy, alkyl, halogen, amino, and alkyl-substituted amino, said method comprising:

(a) providing a starting material having the structural formula (XII)



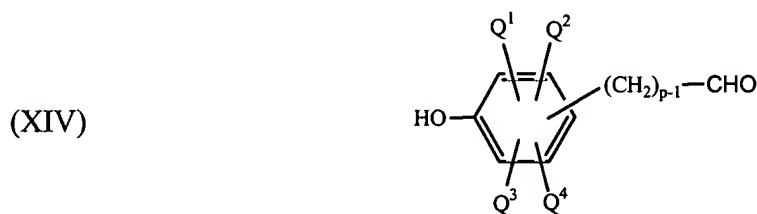
(b) protecting the -OH group and the oxy group with protecting groups, thereby converting the compound into a diene;

(c) deprotecting the oxy group to form a dienone;

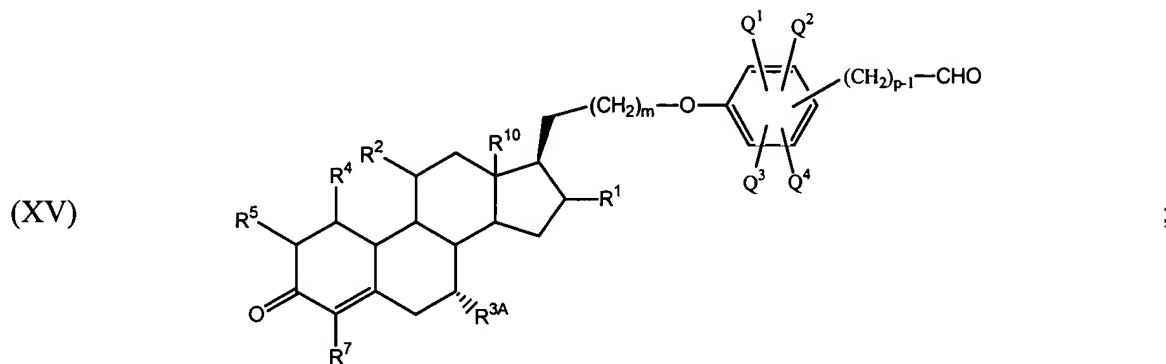
(d) contacting the product of step (b) with an alkyl lithium in the presence of a lithium halide, to provide a  $7\alpha$ -alkyl substituent;

(e) deprotecting the -OH group;

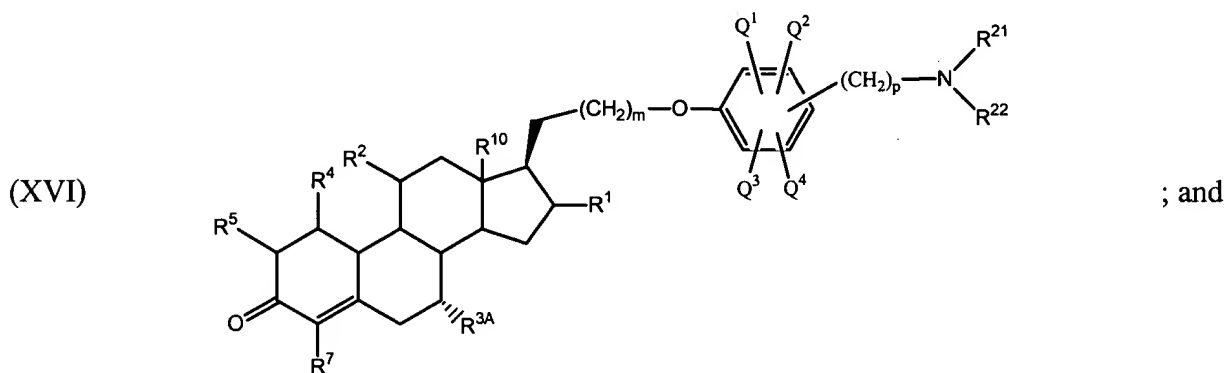
(f) effecting reaction between the -OH group and an aldehyde having the structural formula (XIV)



to result in an intermediate having the structural formula (XV)



(g) treating (XV) with an alkylamine having the structure  $\text{HNR}^{21}\text{R}^{22}$  under reaction conditions effective to produce the amine (XVI)



(h) oxidizing and thereby aromatizing the A ring by reaction with a suitable oxidizing agent or agents.

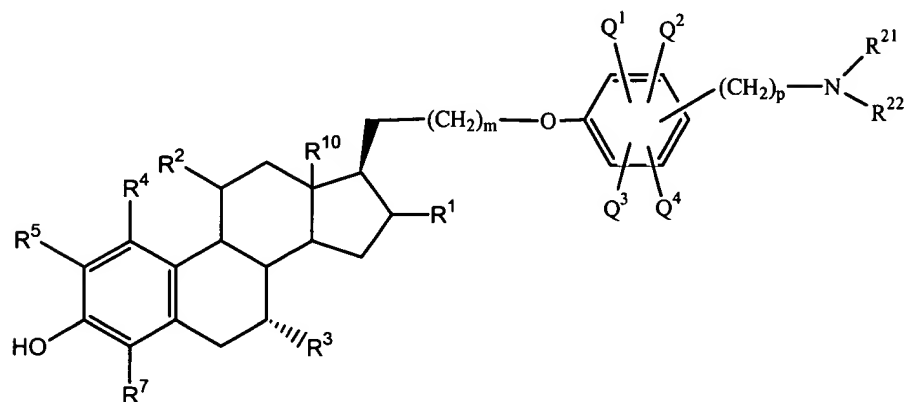
33. The method of claim 32, further including (i) treating the product of step (h) with an acid to produce an acid addition salt.



34. A method for synthesizing an anti-estrogenic steroid having the structural formula

(XI)

(XI)



wherein:

R<sup>1</sup> is CR<sup>11</sup>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> are hydrogen or lower alkyl, and when R<sup>1</sup> is absent, R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is selected from the group consisting of hydrogen, hydroxyl, alkyl, and -OR<sup>13</sup>

wherein R<sup>13</sup> is alkyl;

R<sup>3A</sup> is lower alkyl;

R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> are independently selected from the group consisting of hydrogen and lower alkyl; and

R<sup>10</sup> is methyl or ethyl;

m is zero or 1;

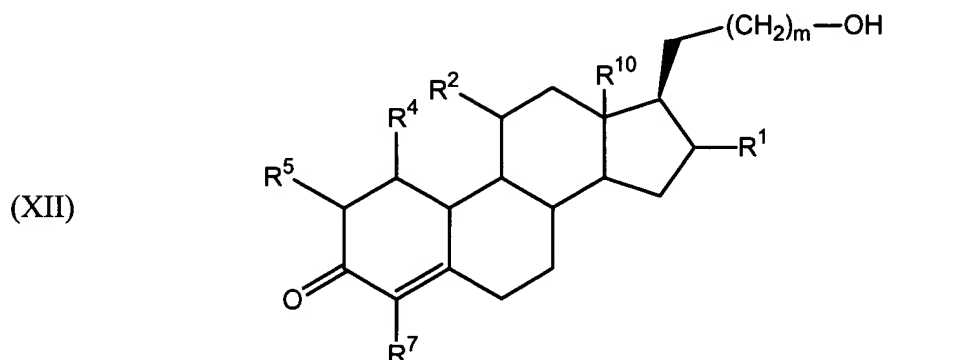
p is an integer in the range of 1 to 7 inclusive;

R<sup>21</sup> and R<sup>22</sup> are lower alkyl or are linked together to form a five- or six-membered heterocycloalkyl ring; and

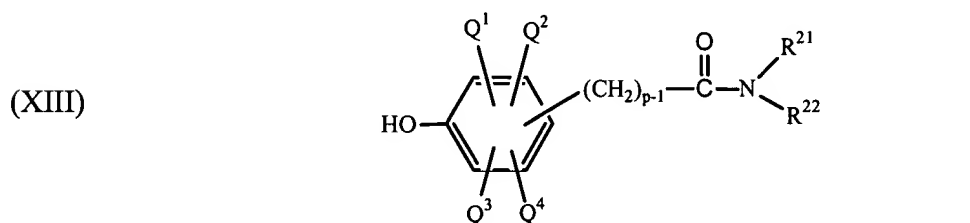
Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup>, and Q<sup>4</sup> are independently selected from the group consisting of hydrogen, hydroxyl, carboxyl, alkoxy, alkyl, halogen, amino, and alkyl-substituted amino,

said method comprising:

(a) providing a starting material having the structural formula (XII)



10 (b) converting the -OH group to an -O-LG moiety wherein LG is a leaving group  
displaceable by nucleophilic attack, and displacing LG by reaction with a hydroxyl-containing  
compound having the structural formula (XIII)



20 (c) oxidizing the A ring to form a diene and protecting resulting the 3-hydroxyl group  
with a protecting group;

(d) converting the protected 3-hydroxyl group into an oxo group, thereby forming a  
dienone;

(e) contacting the product of step (d) with an alkyl lithium in the presence of lithium  
halide, to provide a 7 $\alpha$ -alkyl substituent; and

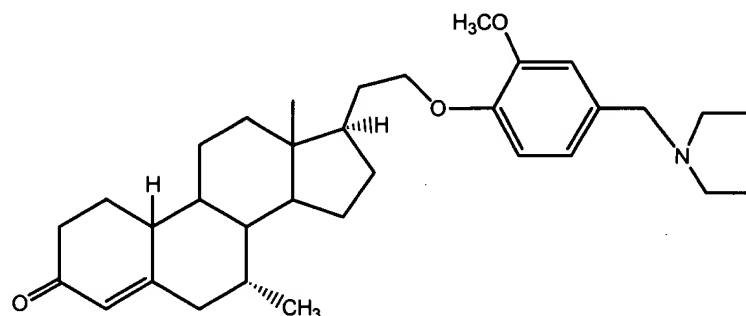
25 (f) reducing the compound so provided to remove all keto moieties.

35. The method of claim 34, further including (g) treating the product of step (f) with  
an acid to produce an acid addition salt.

36. A pharmaceutical composition for administration of a therapeutic agent, comprising a therapeutically effective amount of the compound of claim 20, in combination with a pharmaceutically acceptable carrier.

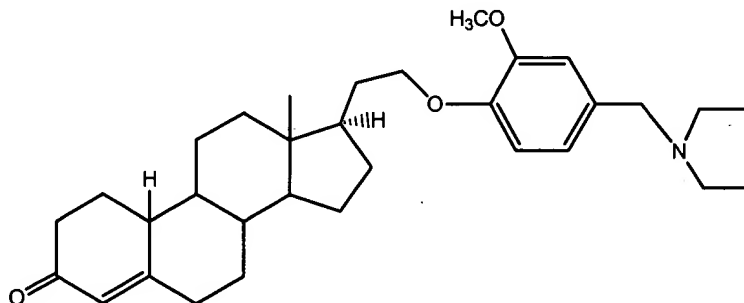
5 37. A pharmaceutical composition for administration of a therapeutic agent, comprising a therapeutically effective amount of the compound of claim 21, in combination with a pharmaceutically acceptable carrier.

10 38. A pharmaceutical composition for administration of a therapeutic agent, comprising a therapeutically effective amount of a compound having the structural formula



15 or a pharmaceutically acceptable acid addition salt thereof, in combination with a pharmaceutically acceptable carrier.

20 39. A pharmaceutical composition for administration of a therapeutic agent, comprising a therapeutically effective amount of a compound having the structural formula



25 or a pharmaceutically acceptable acid addition salt thereof, in combination with a

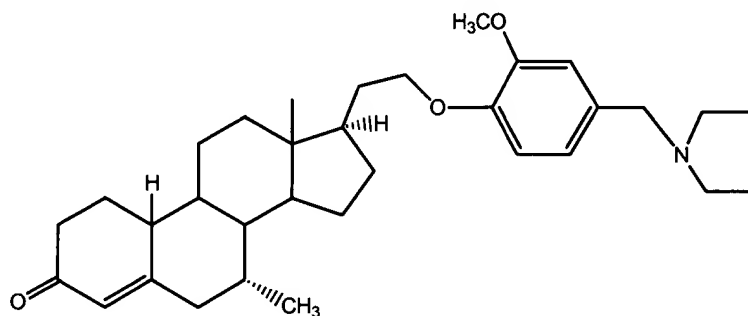
30

pharmaceutically acceptable carrier.

40. A method for treating a human patient suffering from a prostate disorder, comprising administering to the patient, within the context of an effective dosage regimen, a therapeutically effective amount of the compound of claim 20.

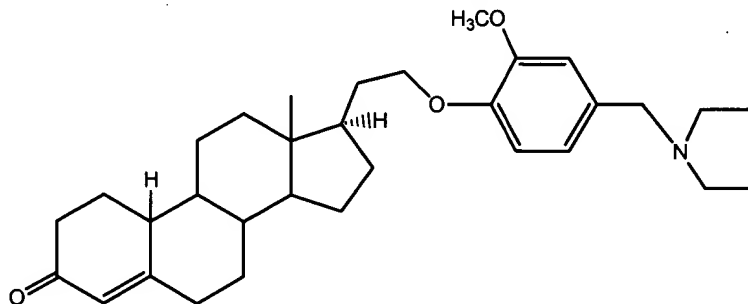
41. A method for treating a human patient suffering from a prostate disorder, comprising administering to the patient, within the context of an effective dosage regimen, a therapeutically effective amount of the compound of claim 21.

42. A method for treating a human patient suffering from a prostate disorder, comprising administering to the patient, within the context of an effective dosage regimen, a therapeutically effective amount of a compound having the structural formula



or a pharmaceutically acceptable acid addition salt thereof.

43. A method for treating a human patient suffering from a prostate disorder, comprising administering to the patient, within the context of an effective dosage regimen, a therapeutically effective amount of a compound having the structural formula



Year	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	

44. A method for stereoselectively adding an alkyl moiety to the 7 $\alpha$  position of a 6 keto steroid comprising providing a C<sup>19</sup> or C<sup>20</sup> tetrahydropyranyl protected hydroxyl moiety on the steroid and reacting the protected steroid with an alkylhalide in the presence of base.